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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61N 5/02, 5/06 — A1

(11) International Publication Number: WO 95/27534

(43) International Publication Date: 19 October 1995 (19.10.95)

(21) International Application Number: PCT/US95/04042

(22) International Filing Date: 7 April 1995 (07.04.95)

(30) Priority Data:
08/224,837 8 April 1994 (08.04.94) US

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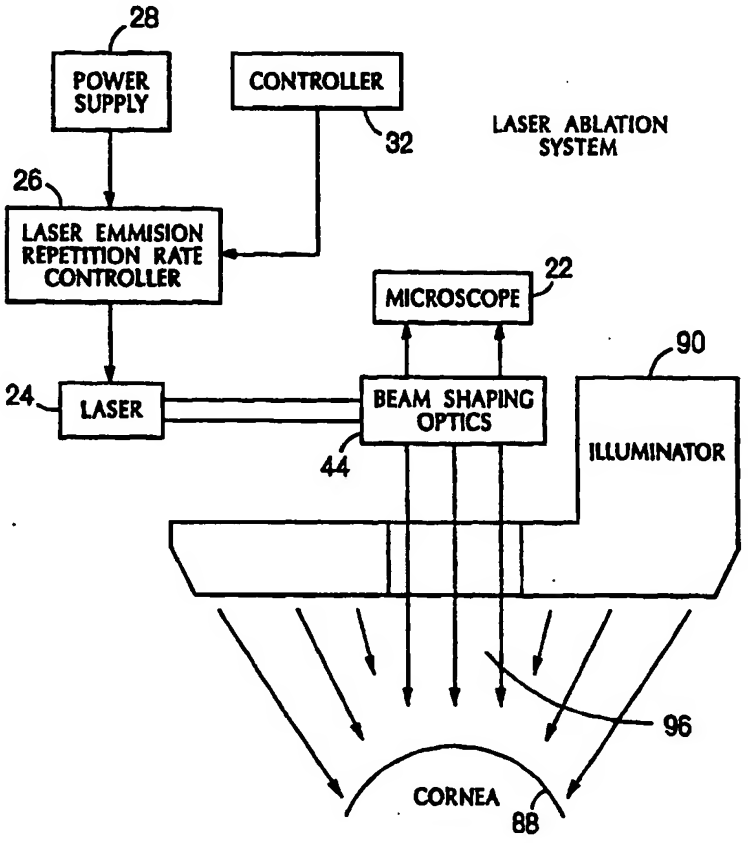
(81) Designated States: AU, BR, CA, JP, KR, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: CONTROL OF PHOTOREFRACTIVE KERATECTOMY

(57) Abstract

A method and system are described for performing photorefractive keratectomy, a desired refractive correction in the corneal tissue. The method and system employ control (32) of the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the desired ablation process while maintaining hydration of the corneal tissue. Controlling the average repetition rate (26) of the radiation pulses (24) applied to the corneal surface so as to reduce intrapulse fluid accumulation at the corneal surface without dehydrating the corneal tissue, selecting an increased fluence level of the pulse applied to the corneal surface to reduce the effect of fluid accumulation at the corneal surface, and applying evaporative energy to the site of incidence of a pulse of an ablative beam prior to incidence of said pulse at said site are shown as ways to effect this control. Application of the new method and system to wide area ablation techniques and to scanning techniques are described.



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CONTROL OF PHOTOREFRACTIVE KERATECTOMY

Background

This invention relates to improvements in photorefractive keratectomy (PRK).

In PRK, corneal tissue is removed in a controlled fashion to shape the surface of the cornea of a patient's eye to treat, e.g., myopia, hyperopia, presbyopia or astigmatism.

The cornea comprises transparent avascular tissue that forms the anterior portion of the eye. The cornea functions as both a protective membrane and a "window" through which light passes as it proceeds to the retina. The transparency of the cornea is due to its uniform structure, avascularity, and deturgescence, which is the state of relative hydration of the corneal tissue.

A major proportion of the refractive power of the eye is determined by the curvature of the anterior surface of the cornea, so that changing the shape of the cornea offers a way to significantly reduce a refractive problem in the eye.

Various techniques have been proposed for shaping the cornea of a patient's eye. The general technique involves removing the epithelium, and then shaping the underlying Bowman's and stroma layers. In PRK, photoablation is employed using e.g., ultraviolet radiation from an excimer laser, e.g. at 193 nm wavelength, or infrared laser radiation that has a wavelength in the range of about 2.9 to 3.2 μm.

In one technique, described in Marshall et al., U.S. Patent No. 4,941,093 (assigned to Summit Technology Inc.), the shape and size of the area of the corneal surface which is irradiated by laser radiation is selected and controlled so that some areas of the corneal

surface become more eroded than others and a desired corneal shape is achieved.

Another technique, described in Muller, U.S. Patent No. 4,856,513 (assigned to Summit Technology Inc.), uses a laser and an erodible mask. The mask, with a predefined profile of resistance to erosion by laser radiation, is disposed between the laser and the corneal surface. A portion of the laser radiation is absorbed by the mask, while another portion is transmitted to the corneal surface in accordance with the mask profile, thereby enabling the selective photoablation of the corneal surface into a desired shape.

There are circumstances in which it is desired to accomplish the PRK treatment with the ablated zone larger than 5 mm in diameter. With such zones, under usual operating conditions it has been observed that the final surface achieved by the ablation process differs from the expected shape. Surface irregularity and significant refractive error has been observed post-operatively in the corneal topographies of some patients treated for PRK. These irregularities may lead to visual disturbances such as diplopia, blurred vision, and loss of Best Corrected Visual Acuity (i.e., the vision obtained with the best possible lens correction).

The PRK procedure has achieved a clinically accepted level. However the possibility of achieving even better results with larger ablation zones has been somewhat elusive. The present invention provides a new insight into conditions that can occur in PRK and provides techniques that address these conditions to enable enhanced predictability, stability, and safety of the procedure to be achieved.

Summary of the Invention

In performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to

selectively ablate corneal tissue of a patient's eye to produce a desired refractive correction in the corneal tissue, particularly when ablating areas larger than about 5.5 mm in diameter, we have realized that improved results can be achieved by controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of this fluid on the ablation process while maintaining hydration of the tissue. The ocular fluid to which we refer is the physiological fluid produced naturally by the eye, which contains various proteins and solutes, and which tends to accumulate in regions subject to photoablation. As the ablation proceeds, solid residues of the preceding ablative process also enter the fluid. The reference to the fluid being "at the corneal surface" refers to liquid on the surface and fluid present among the initial molecules that form the surface structure. By "controlling", we refer to systematic selection or adjustment of parameters of the treatment conditions in a way that takes into account the detrimental effect accumulated ocular fluid can have upon the result of the procedure relative to the correction that is desired, and the need not to dehydrate the remaining corneal tissue.

In addition to recognizing the importance of this step, we have also conceived various approaches for accomplishing the step, some of which can be accomplished by simple adjustment or selection of parameters without affecting the complexity of the procedure or its cost.

In the case of wide-area ablation, in which a pulsed beam of ablative energy of variable controlled diameter is centered on the eye, it is often desired to maintain the fluence of the beam constant from pulse to pulse. We have realized that selection of the repetition rate of the optical pulse may be employed f r controlling the ocular fluid effect. By employing a rate

sufficiently high, in excess of 10 Hz, intrapulse fluid accumulation can be reduced at the surface to be ablated such that the aggregate disturbing effect does not result in a dioptic variation greater than a prescribed amount, for instance 1/4 Diopter. Preferably the effective pulse rate is selected in the range between about 12 to 100 Hz, depending upon other parameters being employed.

In other wide-area ablation systems, the fluence of the pulses may also be selected for the purpose of controlling the effect of intrapulse fluid accumulation without dehydration of the corneal tissue. We have realized that selecting higher beam fluence levels, within a practical operating range, reduces the sensitivity of each beam pulse to intrapulse fluid accumulation. Here, advantage is taken of a saturation trend, i.e. the increase of the amount of material ablated as the fluence increases occurs at a rate that has a decreasing value.

In other systems, the repetition rate and fluence levels employed can both be selected having in mind their effect in respect of the ocular fluid problem. In sophisticated systems employing control by a computer program the values of these parameters may be varied on a case-by-case basis for controlling the effect of ocular fluid accumulation, while avoiding corneal tissue dehydration.

We have also realized that the sensitivity of the ablative process to the effects of ocular fluid accumulation is dependent upon the depth of the tissue being removed. This dependency can be understood from the following considerations. Refractive error of a procedure is typically desired to be held within a prescribed absolute tolerance, or "precision" such as 1/4 Diopter. On the other hand, the disturbance caused by a given value of intrapulse accumulation of ocular fluid is

cumulative, increasing for a given site with the number of pulses that are incident on the site. Furthermore, we have observed that the rate of accumulation of ocular fluid at a site increases with the depth of tissue removed. Likewise the amount of ablative residue in the fluid may increase with the depth of tissue removed. It is realized that if more ocular fluid or fluid with higher, absorptive values exists in some areas than in other areas in the ablation zone, non-uniform ablation will occur with pulses that overlap those areas. Thus the sensitivity of the ablative process to the ocular fluid problem is realized to be dependent upon the depth of tissue removal.

We have further realized it is significant that the depth of tissue removed, for a given Diopter correction, varies as a power function with the diameter of the ablation zone. The degree of disturbance of the ablation attributable to accumulated ocular fluid and the degree of required control on the effects of ocular fluid likewise are found in general to be related to a power function of the diameter of the ablation zone.

According to the invention, based on observations conducted employing beam pulses of 180 mJ cm^{-2} of excimer laser pulses of 193 nm wavelength, the method and system for applying beam pulses of photoablative radiation are preferably selected so that at any given site of incidence of the beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which the beam pulses are provided, the effective average fluence (F, expressed in mJ cm^{-2}) of the beam pulses, and the average diameter (ϕ, expressed in mm) of the ablation zone, have the general relationship:

$$\text{Rep Rate} \geq C \times \phi^2/\ln(F),$$

where C is between 1.5 and 2.0.

Also because the depth of tissue varies with the Diopter value of the correction to be effected in the patient's cornea, for improved control, the system parameters can be selected to take this factor into account as well. Because it is desirable that the precision of the correction be maintained at an absolute value over the range of dioptric corrections, e.g. within 1/4 Diopter, and because small localized variations in tissue depth may have large effect upon the local refractive value, we have realized that the size of the correction in Diopter has greater than a linear effect on the degree of control needed in respect of the ocular fluid problem. According to this realization, the invention also features a method and system in which the beam pulses are so selected that, at any given site of incidence of the beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which the beam pulses are provided, the effective average fluence (F, expressed in mJ cm^{-2}) of the beam pulses, the average diameter (ϕ, expressed in mm) of the ablation zone, and the dioptric power (D, expressed in Diopter) at the location of maximum correction to be effected in the patient's cornea, maintain the general relationship:

$$(\phi^2 \times D^2) \; / \; (\ln(F) \times \text{Rep Rate}) \leq C,$$

where C is about 15. This is based on observations made employing beam pulses of 180 mJ cm^{-2} of excimer pulses of 193 nm wavelength, at a 6 mm diameter ablation zone, for a 5 Diopter correction at 20 Hz pulse rate.

Other techniques to control the effects of accumulating ocular fluid can be used in conjunction with the technique just described or can constitute effective control by themselves.

An evaporative effect provided uniformly can be employed to remove intrapulse accumulation of ocular fluid.

In one case the invention features a double pulse system. Immediately preceding the main pulse at ablating energy level (e.g. fluence between about 100 to 250 mJ cm^{-2} in the case of pulses of 193 nm wavelength in a wide area ablation system), a precursor evaporative pulse of the same wavelength of carefully controlled energy is introduced at fluence below the ablative threshold, e.g. of 50 mJ cm^{-2}. The effect of the precursor pulse is to produce evaporation of accumulated ocular fluid. In order to obtain the evaporation without dehydrating the corneal tissue, the parameters of the precursor beam are selected to limit the depth of the energy deposition.

In another case, a separate source of irradiation is employed which may operate continuously, intermittently, or in pulses at desired times. In one preferred embodiment a CO_2 laser is employed to produce radiation at a wavelength that is highly absorbed by water. The stream of pulses of evaporative energy may advantageously be coordinated to avoid overlap of the incident pulses of evaporative and ablative wavelengths and to optimize the state of reduction of fluid accumulation without tissue dehydration at the time of incidence of the ablative pulse upon a given site.

According to another aspect of the invention, the ambient humidity at the locus of the eye is maintained at a well controlled level below saturation during the procedure to accelerate evaporation of ocular fluid that tends to accumulate. This may include maintaining the room at low humidity or special provisions localized to the region of the eye, such as a gentle, general distribution of gas, at appropriate humidity to cause evaporation of accumulated ocular fluid, via a series of outlets uniformly distributed about the eye.

According to another aspect of the invention, controlling the effect that can be caused by the

accumulation of ocular fluid involves reducing the tendency of the body to present such fluid at the ablative site. This can be effected by systemic or local administration of a drug that is effective to retard the fluid accumulation. Such treatment may be supplemented with control of the general thermal condition of the eye, as by cooling prior to treatment, in manner that retards flow of the ocular fluid to the ablation site.

It will be understood that the degree of control to be employed with respect to any parameter during wide area ablation for controlling the effect of ocular fluid is not to be determined in isolation, but rather out of consideration of the values of other parameters that are employed. Suffice it to say that effective wide area ablation, with ablating zones in excess of about 5.5 mm, up to about 10 mm, and in particular including the range of 6.0 mm to 8.0 mm, can be performed following the present teachings. Specifically, the present invention contributes to solving the problem of "islands" of excess tissue that have been observed as a result of operation of some ablative systems.

In certain broader aspects, the invention equally is relevant to scanning ablative systems in which the ablative beam is narrow in one or both dimensions relative to the dimension of the ablative zone, or is smaller in area than the ablation zone, and in which such beam is displaced laterally from pulse to pulse. In such systems the intrapulse accumulation of ocular fluid relates to the period between which pulses are incident in the same point which is typically at a much lower rate than the pulse rate of the originating laser, due to the distribution of the pulses between many different points in the ablative zone.

The considerations above apply with even greater force in respect of such scanning systems, while the

nature of such systems permit control of additional parameters.

According to the invention, in such systems higher fluence levels can be selected because the opportunity for thermal build up can be reduced by judicious distribution of the pulses. Also, because of the smaller beam size, it is feasible to operate at lower controlled fluence levels. The range of practical fluence levels for scanning-type systems lies between about 80 and 500 mJ cm^{-2}. Likewise the repetition rate of the laser itself may be very high when scanning techniques are employed, while the local effective pulse rate of any site of incidence of the beam may be maintained over a wide range depending upon the selected fluence, but still must be sufficiently frequent, e.g. above 10 Hz, to control the effect of the ocular fluid.

It will be understood that scanning systems enable further degrees of freedom in operation and provide abilities to more readily control the effect of the ocular fluid than are provided by control of the average repetition rate and average fluence of the beam. In a scanning system, one can easily change the size of the spot. Changing the size of the spot while keeping the same total energy in the beam is an easy way to change the fluence from pulse to pulse in a very dramatic way. The repetition rate with which the system fires the pulses can likewise be very different than the repetition rate for a wide area ablation system, and can be varied. Furthermore, a given site in the ablation zone in a scanning system can be revisited by the pulses of the laser on a selected basis. Each of these variables may be implemented according to an appropriate algorithm which addresses the issues of controlling the ocular fluid. For example, according to the invention an algorithm is provided which starts to cut deeper

areas, and re-visits the places which are to be deeply ablated more frequently than the places which are to be shallow-ablated. The shallow-ablated regions can tolerate lower repetition rate and a resultant greater disturbance by ocular fluid per pulse, because of a lesser aggregative effect on the dioptric error. Thus the scanning system provides further degrees of freedom to employ algorithmic control by revisiting places of deeper removal with higher frequency. Such a system automatically compensates and thus distinguishes other algorithms that can be used to treat essentially the entire area over the duration of the procedure.

In certain further respects scanning systems have a greater need to comply to the principles established above. Because the ablation occurs in a distribution of small spots or lines there is the additional possibility of lateral transport of material under the dynamic conditions of scanning and a more detrimental effect can occur if ocular fluid is permitted to accumulate. In the case of certain scanning systems, to avoid this effect, the inventors conceive it to be advantageous for each successive firing of the laser to be directed to a relatively distant, virgin place at which any accumulated fluid has not been recently dynamically disturbed by the previous firing.

These illustrate just some of the greater possibilities which scanning systems offer for controlling the effects of ocular fluid at the corneal surface.

While in medicine the physiology of the eye and its mechanisms are not fully understood at the detailed level, certain observations that lead to further insight into the present invention can be mentioned.

Ocular fluid present in the native cornea that is responsible for maintaining proper hydration of the eye may appear on the surface of the cornea within the boundaries of the treatment zone. Though this fluid is water-based, it contains substantial quantities of proteins and various solutes necessary for proper corneal function. As the corneal lamellae are ablated, ocular fluid may flow out of the stroma and tend to accumulate non-uniformly on the exposed ablated surface. During the course of the ablation treatment, the concentration in the ocular fluid of solid residues of the preceding ablative action can increase. The possibility of redeposit on the corneal surface of fluid cast into space by the ablation process is also possible. Although pure water may have little effect on the ablative beam, the biomaterial present in the fluid can have strong absorption characteristics for the photoablating laser energy used in PRK, and the absorptive character of the fluid can increase as the concentration of ablative residue increases.

It is realized that accumulated ocular fluid, particularly if it covers well the tissue to be ablated can cause the incoming photoablating laser energy to be partially absorbed before reaching the underlying stromal tissue, thereby reducing the fluence available to ablate the corneal tissue and disturbing the rate of ablation. On the other hand, if the stromal tissue is not so completely wetted by the ocular fluid, the ablation can proceed in a manner much less affected by the ocular fluid.

Non-uniform accumulations of ocular fluid over the surface being ablated are therefore detrimental to the photo-ablative process. The step of controlling the effects of accumulated ocular fluid without dehydrating

the tissue solves this problem and enables use of ablative zones larger than 5 cm with improved effect.

Other features and advantages of the invention will become apparent from the following description and from the claims.

Brief Description of the Drawings

Fig. 1 is a side elevational view of a patient undergoing photoablative shaping of corneal tissue.

Fig. 1A is a schematic diagram illustrating the relationship between optical components inside the laser source housing and the optical support assembly shown in Fig. 1.

Figs. 2-2D are elevational schematic views of a patient's cornea at successive times during a conventional PRK procedure.

Figs. 3-3B are elevational schematic views of a patient's cornea at successive times during a PRK procedure according to the invention.

Fig. 4 is a schematic side view of a system employing precursor evaporative pulses preceding ablative pulses during PRK.

Figs. 4A-4F illustrate steps of use of pulses of the precursor beam of subablation energy preceding ablation pulses.

Figs. 5-5D are elevational schematic views of a patient's cornea at successive times during a PRK procedure according to the invention in which an ocular fluid drying beam is employed.

Fig. 6 is an elevational schematic view of a PRK system employing evaporative illumination for controlling accumulated fluid effects.

Figs. 7 and 7A are top schematic views of a pati nt's cornea onto which are projected scannable beam

pulses having a circular beam projection and a long , narrow beam projection, respectively.

Fig. 8 is a flow diagram of a method for performing PRK according to the invention.

Description of the Preferred Embodiments

Referring to Fig. 1, a patient 10, lying on an operating bed 12 with his head restrained between two side supports 14, is shown undergoing photoablative shaping of the cornea in a PRK procedure in accordance with the invention.

An optical support assembly 16 supports beam delivery optics that transmit photoablative radiation from, e.g., a laser source inside housing 18 to beam delivery optics 20. During the cornea shaping procedure, the patient's eye may be observed using a surgical microscope 22.

As shown in Fig. 1A, the laser source housing 18 includes a laser 24 (e.g., an EXCIMED™ ArF excimer laser (193 nm) available from Summit Technology, Inc. of Watertown, MA U.S.A.; other lasers may also be used such as HF, pulsed CO_2, infrared lasers at wavelengths of about 2.6-3.2 μm, Er:YSGG and Er:YAG lasers) that is controlled by a laser emission repetition rate controller 26, and powered by a power supply 28. A laser beam attenuator 30 is employed to control the fluence of the laser pulses delivered from laser 24.

A controller 32 (e.g., a commercially available microprocessor-based computer) choreographs the PRK procedure based upon the parameters of zone size (34) and Diopter correction (36) which are selected by the PRK surgeon based upon the needs of patient 10. As described in detail below, based upon the input information, controller 32 optimizes the average pulse rate and the

average pulse fluence for beam pulses 38 that are delivered to the patient's cornea.

A feedback device 40, such as a profilometer or keratometer (e.g., a PHOTOKERATOSCOPE™ manufactured by Sun Contact Lens Company of Kyoto, Japan, or a CORNEASCOPE™ manufactured by International Diagnostic Instruments Limited, Broken Arrow, Okla. U.S.A.), sends signals to the controller via a feedback path 42, for precise control of the laser during the photoablation procedure.

Beam-shaping optics 44 provide a beam of a desired shape and dimension to an optical delivery system housed within optical support assembly 16. The beam-shaping optics may not always be necessary, should the laser output beam be directly usable. However, with most lasers it will normally be desirable to perform some initial shaping of the beam. For example, some types of laser systems produce beams with rectangular cross-sections (e.g., excimer lasers) and it will normally be preferable to form the beams into square or circular cross-sections.

As mentioned above, it has been discovered that under certain conventional PRK conditions, detrimental phenomena may occur that can affect the accuracy and predictability of PRK procedures.

Referring to Figs. 2-2D, under conventional PRK conditions the pulse rate and fluence levels of the photoablative beam pulses are not optimized, and the resulting accumulation of fluid in the treatment zone can detrimentally affect the outcome of the PRK procedure.

Fig. 2 shows an initial beam pulse 46 and the resulting depth of the removed corneal tissue in an ablation zone 48. As shown schematically in Fig. 2A, if the time between pulses is not short on the time-scale of

corneal fluid perfusion, which has been experimentally observed to be on the order of about 1 second, ocular fluid 50 from the patient's eye can accumulate in ablation zone 48.

Referring to Fig. 2B, ocular fluid 50 can detrimentally affect the ablation uniformity of a subsequent laser beam pulse 52, which is incident upon ablation zone 54, which includes ablation zone 48, by non-uniformly altering the fluence that ultimately reaches the corneal surface as a result of the radiation absorption characteristics of the ocular fluid. Accordingly, a non-uniform corneal surface feature, in the shape of a bump 56, is created in ablation zone 54 by pulse 52. Subsequently, additional fluid 58 can accumulate in ablation zone 54, thereby causing additional non-uniform corneal surface features to be created. As shown in Fig. 3D, the final corneal shape resulting from PRK under such conditions can be rough with final surface features 60 having dimensions on the order of 1-10 μm.

It is to be appreciated that the drawings presented herein are shown schematically for ease of visualization, and that in actual PRK procedures the sharp, cliff-like features shown in these drawings would not be present, and instead smooth transition regions would be present between the different ablation zones.

Assuming the corneal fluids have an absorption coefficient in the range of 3000-5000 cm^{-1}, for low pulse rates, enough ocular fluid could accumulate between successive beam pulses to cause attenuation in the laser beam of about 5% in the region of fluid accumulation. Non-uniform accumulation of such fluid in the treatment zone would cause a difference in the corneal tissue removal rate of 0.01-0.02 μm/pulse, relative to the

removal rate expected for un-attenuated fluence levels, resulting in a cumulative error effect.

In conventional PRK practiced by Summit Technology Inc., in the past, for zone sizes of about 5 mm, beam pulse fluence levels of about 180 mJ/cm^2, and repetition rates of about 10 Hz, no significant non-uniformities in ablation have been observed for up to 5 Diopters of ablation. However, as the zone diameter is increased beyond about 5.5 mm (e.g., between about 6 and 10 mm) the inventors have discovered the importance of addressing the effects of fluid accumulation which if permitted to occur during PRK might cause non-uniform ablation resulting in an error in the final corneal shape which may degrade to some extent the final visual outcome. For instance, in treating a zone size of 6 mm, with 5 Diopter myopic correction, using a fluence level of about 180 mJ cm^{-2}, it was discovered that shifting the effective pulse rate of the laser to 20 Hz, surprisingly produced a significantly improved result in achieving the desired correction and without hazing that would be attributable to dehydration of the corneal tissue.

Following such observations, the inventors have provided a number of approaches for controlling the effects of ocular fluid accumulation in the patient's cornea in a manner substantially preventing the ocular fluid in the ablation area from affecting the photoablation of the patient's cornea during the PRK procedure, while preserving hydration of the corneal tissue.

Referring to Figs. 3-3B, according to the invention, the beam pulse rate is optimally selected, within a practical operating range, to minimize the detrimental eff cts of fluid accumulation in the treatment zone.

As shown in Fig. 3, an initial beam pulse 62 removes a substantially known depth of corneal tissue in an ablation zone 64 in a patient's cornea 66. Referring to Fig. 3A, a subsequent beam pulse 68 is incident upon cornea 66, in an ablation zone 70 that includes initial ablation zone 64, in a time before a substantial amount of ocular fluid could accumulate in zone 64. Thus, beam pulse 68 is capable of uniformly ablating a substantially predetermined depth into cornea 66. As shown in Fig. 3B, the shape of the corneal surface resulting from PRK performed according to the invention is substantially smooth in the treatment zone size with a diameter between about 6 and 10 mm.

Particularly for wide-area ablation procedures, the beam pulse fluence levels are preferably fixed within a fluence range of about 100 to 250 mJ cm^{-2}. A more preferred range under present operating conditions is 170 to 190 mJ cm^{-2}. In the presently most preferred embodiments, the beam fluence is about 180 mJ cm^{-2}. In these procedures, only the repetition pulse rate is optimally selected so that detrimental intrapulse fluid accumulation is substantially avoided. Preferably, the beam pulse repetition rate is controlled by a control switch operating at an effective average repetition rate between about 12 to 100 Hz.

As mentioned above, the effective average rate (Rep Rate, expressed in Hz) at which the beam pulses are provided to a specific site, the effective average fluence (F, expressed in mJ cm^{-2}) of the beam pulses, and the average diameter (ϕ, expressed in mm) of the ablation zone, have the general relationship:

$$\text{Rep Rate} \geq C \times \phi^2/\ln(F)$$

where C is between 1.5 and 2.

In certain preferred embodiments, the fluence level of each beam pulse 62, 68 is also optimally

selected, within a practical range, to minimize the above-mentioned fluid accumulation effect.

Suitable irradiation intensities (i.e., fluence value) are selected based upon the wavelength of the laser radiation and the nature of the irradiated surface. For any given wavelength of laser radiation applied to the corneal layers, there is typically a threshold value of energy density below which significant ablation does not occur. Above this threshold density, there will be a range of energy density over which increasing energy densities provide increasing depths of ablation, until a saturation point is reached, above which no significant increase in ablation rate occurs.

Typically, under conventional PRK conditions, the laser system is used to provide an ideal fluence level at the corneal surface that is slightly less than the saturation value. For example, when ablating the cornea with radiation having a wavelength of 193 nm, using wide area ablation techniques, it is preferable to provide pulses of radiation that have ideal energy densities. Typically, a single pulse with this fluence level will ablate a depth of corneal tissue in the range of about 0.1 to 0.3 μm.

However, according to the invention, for a given radiation wavelength, fluence values greater than the ideal value are used to reduce the sensitivity of each pulse to fluid that may accumulate in the ablation zone. The fluence level is preferably selected so that the amount of fluid that accumulates in the ablation zone between successive pulses absorbs an amount of beam fluence equal to the additional fluence above the ideal value. This selection is based, in part, upon a desire not to unnecessarily heat the corneal surface. According to this scheme, the additional fluence does not cause significant additional ablation in the corneal regions in

which fluid has not accumulated, and instead only serves, in effect, to remove accumulated ocular fluid from the ablation zone without dehydration of the tissue.

For wide area ablation, fluence up to about 250 mJ cm^{-2} may be employed. In scanning systems with smaller beam size, fluence of a pulse can start as low as about 80 mJ cm^{-2}, but may be increased significantly with an upper limit as high as about 500 mJ cm^{-2}, depending on other parameters, for controlling the effect of accumulated fluid.

Because the sensitivity of the procedure varies as a power function with the Diopter value of the correction to be effected in the patient's cornea, for improved control, the system parameters can be selected to take this factor into account as well.

According to this realization, the beam pulses are so selected that, at any given site of incidence of the beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which the beam pulses are provided, the effective average fluence (F, expressed in mJ cm^{-2}) of the beam pulses, the average diameter (ϕ, expressed in mm) of the ablation zone, and the dioptric power (D, expressed in Diopter) at the location of maximum correction to be effected in the patient's cornea at the location of the maximum correction, maintain the general relationship:

$$(\phi^2 \times D^2) / (\ln(F) \times \text{Rep Rate}) \leq C,$$

where C is about 15.

In certain other embodiments, the excess fluid that accumulates in the ablation area is substantially evaporated during the during PRK by applying non-photoablative beam pulses to the corneal surface.

Referring to Fig. 4, in one embodiment according to this scheme, the fluence level of the actual

photoablative beam pulses 72 (e.g., from an excimer laser) are preceded by precursor pulses 74 below the intensity level required for corneal photoablation. The intensity level is maintained in the precursor pulses sufficiently high to substantially evaporate excess fluid that may accumulate so that the ablating pulses are substantially unaffected by accumulated ocular fluid. Figures 4A through 4F illustrate various stages of this procedure.

Alternatively, as shown in Figs. 5-5D, pulses of infra-red radiation 80, 84 (e.g., from a pulsed CO_2 laser) of a wavelength selected to correspond with a peak in the wavelength-absorption profile of water can be employed to substantially evaporate the excess water accumulation in the ablation area during the PRK procedure. The amount of infrared radiation acting on a given volume at the surface, determined by wavelength, fluence, pulse duration and pulse rate, is selected to enhance evaporation of the ocular fluid. The wavelength of this radiation is selected to limit the absorption depth, for instance, to less than 100μ. For this purpose, a wavelength of about 10μ or 294μ or another wavelength corresponding to strong resonant absorption of water is selected. The infra-red beam cross-section is preferably shaped to substantially correspond to the ablation area, although in other embodiments restricting the beam to those regions tending to accumulate the most ocular fluid (central region in case of myopic correction; annular region in case of hyperopic correction) is employed. The pulses of infrared radiation 80, 84 are preferably delivered in a sequence that alternates with the incidence of the photoablative beam pulses 82, 86 on the surface of the ablation area. Alternatively, infrared puls s can be delivered to the treatment zone at twice the rate of the photoablative

pulses, as shown in the drawings. As shown in Fig. 5D, the shape of the resulting surface is substantially smooth using this technique.

In an alternative embodiment, shown in Fig. 6, the effect of ocular fluid across the ablation area can be controlled by controlled application of evaporative energy to the anterior surface of a patient's cornea 88 by using a source 90 of illumination 92 having a sufficient intensity and a wavelength selected to be preferentially absorbed by the anterior 100 μm of corneal tissue. The power intensity of illumination 92 is preferably selected to be about 10 mJ cm^{-2}, or greater. As shown, source 90 preferably has an aperture, not shown, through which beam pulses 96 of photoablative radiation passes. Illumination 92 is preferentially delivered only to the treatment zone on the corneal surface to avoid unnecessary heating of the patient's eye.

Referring to Figs. 7 and 7A, in two alternative embodiments according to the invention, the projection of the photoablating radiation onto corneal treatment zones 98, 100, are selected, at least in one dimension, to be substantially less than the average diameter of the respective zones.

Referring to Fig. 7, a circular projection 102 of a beam pulse is incident upon surface 98. The location of the projection of each successive beam pulse is scanned across the treatment zone, as shown in phantom, until the corneal surface is shaped in the desired manner.

Alternatively, referring Fig. 7A, a long, narrow projection 104 is incident upon corneal surface 100. The long dimension of projection 104 is preferably shorter than the average diameter of treatment zone 100. Projection 104 is scanned across treatment zone 104 in

the direction indicated by double-headed arrow 106, until the corneal surface is properly shaped. The intensity profile across projection 104 is preferably modified in a manner enabling the desired shaping of the treatment zone.

Using the beam projections shown in Figs. 7 and 7A, computer algorithms, as indicated above, can be employed to particular advantage. In one instance, the regions of the deeper tissue removal can be revisited more frequently to limit the intrapulse fluid accumulation to a higher degree than that employed in more shallow regions, thus to provide a more uniform removal of the tissue during the ablative process according to the prescribed correction. Similarly, the controller can alternate the locations of the site of incidence of successive pulses so that dynamic disturbances do not affect succeeding pulses.

Referring to Fig. 8, in an exemplary method of performing PRK according to the invention, a surgeon enters into controller 32, a desired photoablative beam pulse fluence range (110), a desired treatment zone size (112), and a desired Diopter of corneal correction (114) for a given patient. A computer program running within controller 32 computes an optimal beam pulse rate and beam fluence, within the specified range (116). Controller 32 also compute the required number of pulses to achieve the desired Diopter refractive correction in the patient (118) on a conservative basis that avoids over correction. The controller outputs the computed repetition pulse rate to the laser emission repetition rate controller 26 and the computed fluence level to laser beam attenuator 30 (120). Laser source 24 then delivers the required number of pulses to the patient's cornea. Feedback device 40 measures the shape of the corneal surface and relays this information to the

controller (124). If the shape is within the desired correction (126), the procedure terminates (128). However, if further correction is required, the controller re-computes the required number of pulses to achieve the desired Diopter refractive correction (118).

In certain embodiments, drugs can be topically applied to the cornea to regulate and reduce the release of corneal fluids so as to control the uniformity of corneal hydration during PRK. Preferred ocular fluid-controlling drugs include phenol-barbital and carbonic-anhydrase inhibitors such as acetazolamide which has an inhibiting effect on fluid proliferation.

It should be noted that further preferred embodiments employ selected combinations of the above-described schemes, depending upon the parameters of the system, in order to avoid non-uniform material removal problems. The combinations are selected to achieve more predictable and accurate results.

The further features described in an application entitled Improvements in Photo-Refractive Keratectomy, filed contemporaneously herewith, and assigned to Summit Technology Inc. to whom the present invention is assigned, the contents of which are hereby incorporated by reference, can also be combined with useful effect with the features taught here.

CLAIMS

1. In a method for performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to selectively ablate corneal tissue of a patient's eye in an ablation zone on the anterior corneal surface, having an average diameter in excess of 5.5 mm, to produce a desired refractive correction in the corneal tissue, the improvement comprising:

controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the desired ablation process while maintaining hydration of the corneal tissue.

2. The method of claim 1 wherein said step of controlling the effect of ocular fluid further comprises controlling the average repetition rate of the radiation pulses applied to the corneal surface so as to reduce intrapulse fluid accumulation at the corneal surface without dehydrating the corneal tissue.

3. The method of claim 1 wherein said step of controlling the effect of ocular fluid comprises selecting an increased fluence level of the pulse applied to the corneal surface to reduce the effect of fluid accumulation at the corneal surface.

4. The method of claim 1 wherein said step of controlling the effect of ocular fluid comprises applying evaporative energy to the site of incidence of a pulse of an ablative beam prior to incidence of said pulse at said site.

5. In a method for performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to selectively ablate corneal tissue of a patient's eye in an ablation zone on the anterior corneal

surface, having an average diameter in excess of 5.5 mm, to produce a desired refractive correction in the corneal tissue, the improvement comprising:

controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the desired ablation process while maintaining hydration of the corneal tissue comprising performing the procedure with pulses of radiation at a repetition rate greater than 10 Hz when the maximum ablation zone exceeds about 5.5 mm in diameter or the refractive correction exceeds about 5 Diopters in refractive power.

6. The method of claim 2 or 5 wherein said average repetition rate at points of incidence of said beam within the ablative zone is controlled within a range of 12 to 100 Hz.

7. In a system for performing photorefractive keratectomy employing pulses of photoablative radiation to selectively ablate corneal tissue of a patient's eye in an ablation area on the anterior corneal surface to produce a desired refractive correction in the corneal tissue, the improvement comprising:

ocular fluid control means for controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the ablation process while maintaining hydration of the corneal tissue.

8. The system of claim 6 wherein said ocular fluid control means comprises means for controlling the repetition rate of the radiation pulses applied to the corneal surface so as to reduce intrapulse fluid accumulation at the corneal surface.

9. The system of claim 8 wherein the means for controlling the repetition rate of the radiation pulses comprises means for calculating the optimal repetition rate for a given maximum ablation zone size.

10. The system of claim 8 wherein the means for controlling the repetition rate of the radiation pulses further comprises means for calculating an optimal repetition rate for a given refractive correction.

11. The system of claim 8 wherein the means for controlling the repetition rate of the radiation pulses further comprises a control switch operating at a repetition rate between about 12 to 100 Hz.

12. A method for performing photorefractive keratectomy to produce a desired refractive correction in the cornea of a patient's eye, said method comprising the steps of

providing multiple, successive beam pulses of radiation from an excimer laser for removing corneal tissue from the patient's eye by photoablation, and

applying said pulses to the patient's cornea, over an ablation zone with a diameter in excess of 5.5 mm, at an average rate selected to be sufficiently rapid, and at sufficiently high fluence, that the effect of the ablation produced during each pulse, at its respective site of incidence, substantially prevents detrimental accumulation of ocular fluid at said site, before the next beam pulse arrives at the same site, which would otherwise present risk of causing sufficient non-uniformity in the photoablative removal of tissue, over the course of the PRK procedure, that the desired refractive correction is detrimentally affected.

13. The method of claim 12 wherein said step of applying said pulses comprises the step of providing beam pulses selected so that at any given site of incidence of said beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which said beam pulses are provided, the effective average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, and the average diameter (ϕ, expressed in mm) of the ablation zone, have the general relationship:

$$\text{Rep Rate} \geq C \times \phi^2 / \ln(F)$$

where C is between about 1.5 and 2.0.

14. The method of claim 12 wherein said step of applying said pulses comprises the step of providing beam pulses selected so that, at any given site of incidence of said beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which said beam pulses are provided, the effective average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, the average diameter (ϕ, expressed in mm) of the ablation zone, and the dioptric power (D, expressed in Diopter) of the correction to be effected in the patient's cornea at the location of the maximum correction, maintain the general relationship:

$$(\phi^2 \times D^2) \; / \; (\ln(F) \times \text{Rep Rate}) \leq C,$$

wherein the value of C is about 15.

15. The method of claim 13 or 14 adapted to perform wide area ablation and wherein said step of applying said pulses comprises providing said beam pulses with an average fluence, at the ablation zone, in the range of 100-250 mJ cm^{-2}.

16. The method of claim 15 wherein the wavelength of said beam is 193 nm.

17. The method of claim 16 wherein the fluence of the pulse is between about 170 and 190 mJ cm^{-2}.

18. The method of claim 17 wherein the fluence is about 180 mJ cm^{-2}.

19. The method of claim 13 or 14 adapted to perform ablation using a scanning technique and wherein said step of applying said pulses comprises providing said beam pulses with an average fluence, at the ablation zone, in the range of 80 to 500 mJ cm^{-2}.

20. The method of claim 12 wherein said step of applying said pulses comprises the steps of

providing said beam pulses in a form that has a projection onto the ablation zone that is smaller in area than the overall ablation zone, and

scanning said beam pulses across the ablation zone until the desired refractive correction is produced in the patient's cornea.

21. The method of claim 12 wherein said step of applying said pulses comprises the steps of

providing said beam pulses in a form that has a projection onto the ablation zone that, in least one dimension, is substantially smaller than the average diameter of the ablation zone, and

scanning beam pulses across the ablation zone until the desired refractive correction is produced in the patient's cornea.

22. The method of claim 21 wherein each of said beam pulses is provided in a form that has a circular projecti n onto the ablation zone.

23. The method of claim 21 wherein each of said beam pulses is provided in a form that has a long, narrow projection onto the ablation zone, wherein the long dimension of said projection is longer than the average diameter of the ablation zone.

24. The method of claim 21 wherein said scanning is a progressive scan covering the entire surface to be ablated before repeating.

25. The method of claim 21 wherein said scanning places the beam at spaced locations in successive scans.

26. The method of claim 21 wherein said scanning is accomplished at higher and lower repetition rates at regions at which respectively deeper and less deep regions of tissue are being ablated in the course of the PRK procedure.

27. The method of claim 1 or 12 wherein said step of applying said beam pulses comprises the step of applying said beam pulses to an ablation zone having a diameter between about 6 and 10 mm.

28. The method of claim 12 wherein said step of applying said beam pulses comprises the step of applying said pulses to the patient's cornea in a manner selected to correct a myopic condition.

29. The method of claim 12 wherein said step of applying said beam pulses comprises the step of applying said pulses to the patient's cornea in a manner selected to correct a hyperopic condition.

30. The method of claim 12 wherein said step of applying said beam pulses comprises the step of applying said pulses to the patient's cornea in a manner selected to correct an astigmatic condition.

31. The method of claim 12 wherein said step of applying said beam pulses comprises the step of applying said pulses to the patient's cornea in a manner selected to correct at least two conditions selected from the group consisting of myopia, hyperopia, presbyopia and astigmatism.

32. A method for performing photorefractive keratectomy to produce a desired refractive correction in the cornea of a patient's eye, said method comprising the steps of

providing multiple, successive beam pulses of ablative radiation for removing corneal tissue from the patient's eye by photoablation, and

applying said pulses to the patient's cornea, over an ablation zone with a diameter in excess of 5.5 mm, at an average rate selected to be sufficiently rapid, and at sufficiently high fluence, that the effect of the ablation produced during each pulse, at its respective site of incidence, substantially prevents detrimental accumulation of ocular fluid at said site, before the next beam pulse arrives at the same site, which would otherwise present risk of causing sufficient non-uniformity in the photoablative removal of tissue, over the course of the PRK procedure, that the desired refractive correction is detrimentally affected.

33. In a method for performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to selectively ablate corneal tissue of a

patient's eye in an ablation zone on the anterior corneal surface, having an average diameter in excess of 5.5 mm, to produce a desired refractive correction in the corneal tissue, the improvement comprising:

controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the ablation process,

said method of controlling the effect of said ocular fluid comprising administering to the patient a drug that reduces the tendency for ocular fluid to accumulate at said ablation site.

34. In a method for performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to selectively ablate corneal tissue of a patient's eye in an ablation zone on the anterior corneal surface, having an average diameter in excess of 5.5 mm, to produce a desired refractive correction in the corneal tissue, the improvement comprising:

controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the ablation process,

said method of controlling the effect of said ocular fluid comprising regulating the temperature of the eye upon which the treatment is performed.

35. In a method for performing a photorefractive keratectomy procedure employing pulses of photoablative radiation to selectively ablate corneal tissue of a patient's eye in an ablation zone on the anterior corneal surface, having an average diameter in excess of 5.5 mm, to produce a desired refractive correction in the corneal tissue, the improvement comprising:

controlling the effect of ocular fluid at the corneal surface so as to reduce the disturbance of such fluid on the ablation process,

said method of controlling the effect of said ocular fluid comprising regulating the ambient humidity to a lower value than general ambient conditions at the eye upon which the treatment is performed.

36. A system for performing photorefractive keratectomy to produce a desired refractive correction in the cornea of a patient's eye, said apparatus comprising

an excimer laser for providing multiple, successive beam pulses of radiation for removing corneal tissue from the patient's eye by photoablation,

a beam pulse delivery system, disposed between said laser and the patient's eye, for applying said pulses to the patient's cornea, over an ablation zone with a diameter in excess of 5.5 mm, and

beam pulse controlling means for selectively controlling the average rate said beam pulses are delivered to the ablation zone to be sufficiently rapid, and at sufficiently high fluence, that the effect of the ablation produced during each pulse, at its respective site of incidence, substantially prevents detrimental accumulation of ocular fluid at said site, before the next beam pulse arrives at the same site, which would otherwise present risk of causing sufficient non-uniformity in the photoablative removal of tissue, over the course of the PRK procedure, that the desired refractive correction is detrimentally affected.

37. The system of claim 36 wherein said controlling means is constructed and arranged to provide beam pulses selected so that, at any given site of incidence of said beam pulses in the ablation zone, the

average rate (Rep Rate, expressed in Hz) at which said multiple, successive beam pulses are provided, the average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, and the average diameter (ϕ, expressed in mm) of the ablation zone, have the general relationship:

$$\text{Rep Rate} \geq C \times \phi^2/\ln(F)$$

where C is between 1.5 and 2.

38. The system of claim 36 wherein said controlling means is constructed and arranged to provide beam pulses selected so that, at any given site of incidence of said beam pulses in the ablation zone, the average rate (Rep Rate, expressed in Hz) at which said beam pulses are provided, the average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, the average diameter (ϕ, expressed in mm) of the ablation zone, and the dioptric power (D, expressed in Diopter) of the correction to be effected in the patient's cornea, at the location of the maximum correction, the following general relationship is maintained:

$$(\phi^2 \times D^2) / (\ln(F) \times \text{Rep Rate}) \leq C$$

where C is about 15.

39. A system for performing photorefractive keratectomy to produce a desired refractive correction in the cornea of a patient's eye, said apparatus comprising

an excimer laser for providing multiple, successive beam pulses of radiation for removing corneal tissue from the patient's eye by photoablation,

a beam pulse delivery system, interposed between said laser and the patient's eye for applying said pulses to the patient's cornea, over an ablation zone with a diameter in excess of 5.5 mm, and

beam pulse controlling means for selectively controlling the average rate (Rep Rate, expressed in Hz)

at which said beam pulses are delivered to the ablation zone, and for selectively controlling the average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, so that, for a given average ablation zone diameter (ϕ, expressed in mm), the following general relationship is maintained:

$$\text{Rep Rate} \geq C \times \phi^2/\ln(F)$$

where C is between 1.5 and 2.

40. The system of claim 39 wherein said beam pulse controlling means is further adapted to control the average rate (Rep Rate, expressed in Hz) at which said beam pulses are delivered to the ablation zone and the average fluence (F, expressed in mJ cm^{-2}) of said beam pulses, so that for a given dioptric power (D, expressed in Diopter) to be effected in the patient's cornea, at the location of the maximum correction, the following general relationship is maintained:

$$(\phi^2 \times D^2) / (\ln(F) \times \text{Rep Rate}) \leq C$$

where the value of C is about 15 .

41. A system for performing photorefractive keratectomy to produce a desired refractive correction in the cornea of a patient's eye, said apparatus comprising

a source of ablative radiation for providing multiple, successive beam pulses of radiation for removing corneal tissue from the patient's eye by photoablation,

a beam pulse delivery system, disposed between said source and the patient's eye, for applying said pulses to the patient's cornea, over an ablation zone with a diameter in excess of 5.5 mm, and

beam pulse controlling means for selectively controlling the average rate said beam pulses are delivered to the ablation zone to be sufficiently rapid, and at sufficiently high fluence, that the effect of the

ablation produced during each pulse, at its respective site of incidence, substantially prevents detrimental accumulation of ocular fluid at said site, before the next beam pulse arrives at the same site, which would otherwise present risk of causing sufficient non-uniformity in the photoablative removal of tissue, over the course of the PRK procedure, that the desired refractive correction is detrimentally affected.

42. A PRK scanning system constructed to ablate selected areas to remove a greater depth of tissue than at other selected areas, said system controlled by an algorithm that causes revisiting the areas of the ablative zones from which the greater depth of tissue is to be removed with greater frequency than are visited the other selected areas.

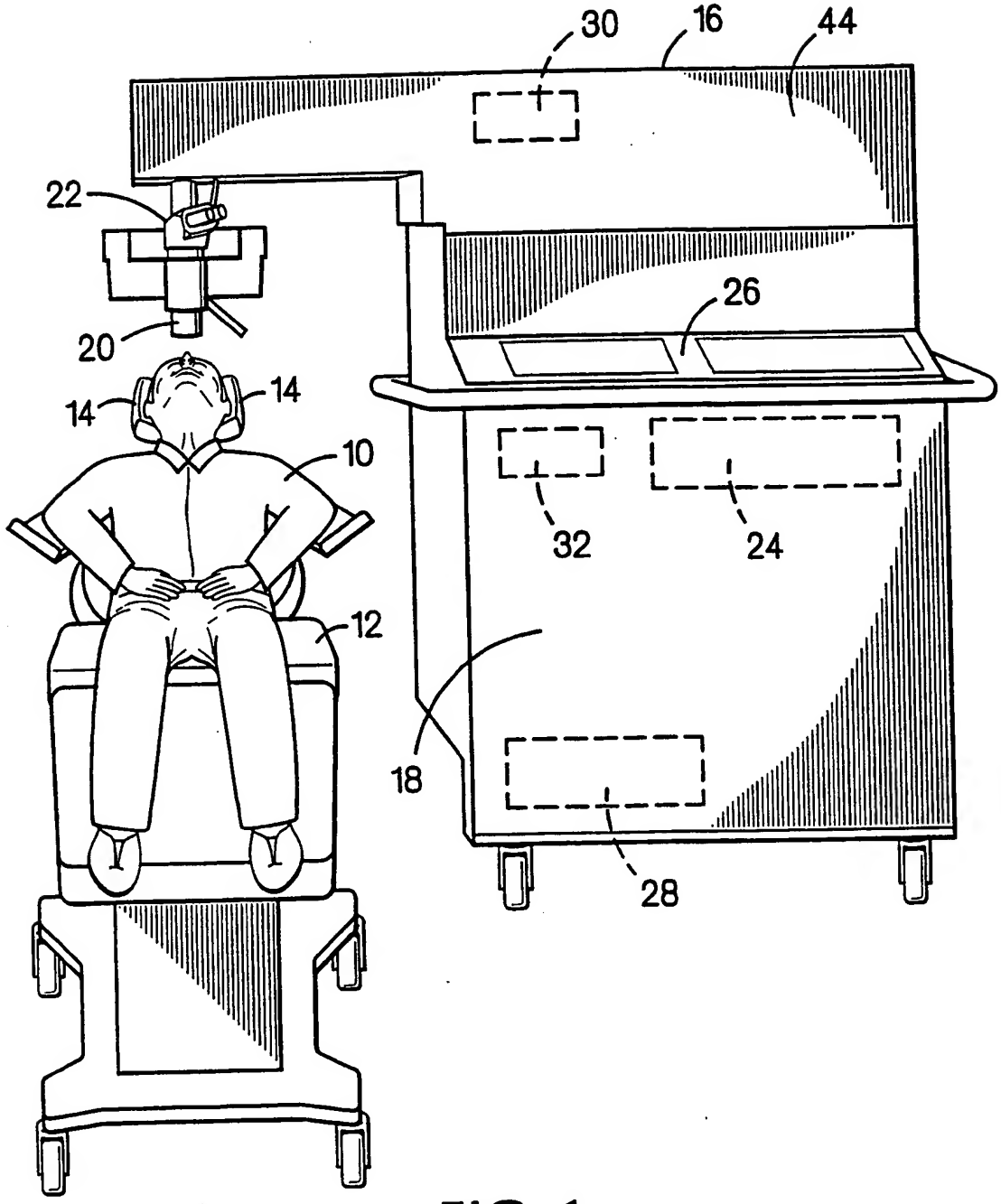

FIG. 1

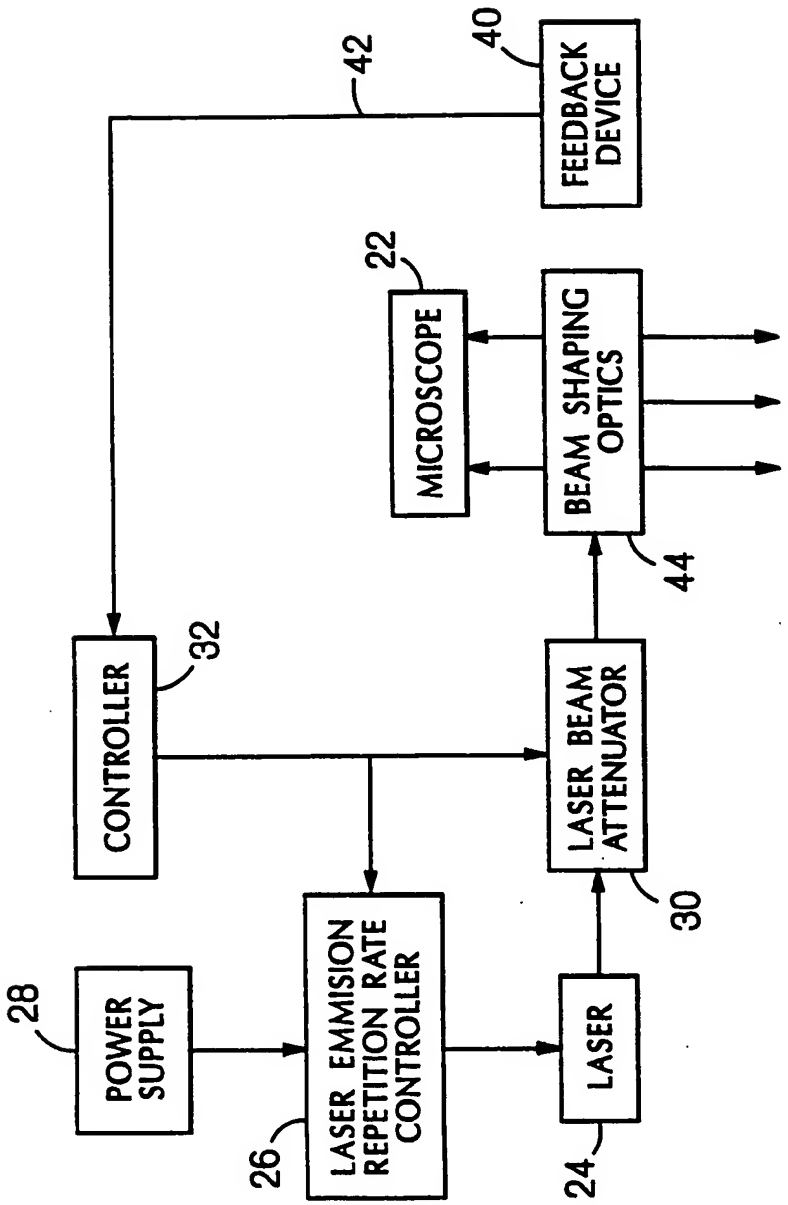

FIG. 1A

FIG. 2

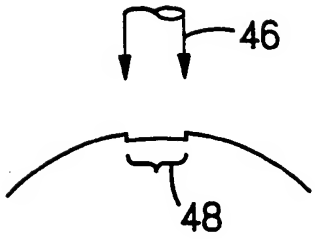

FIG. 2A

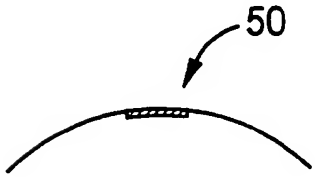

FIG. 2B

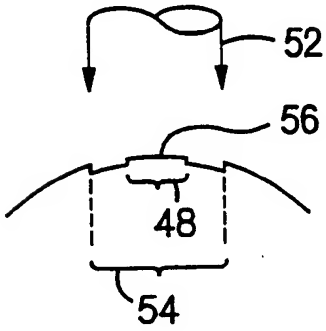

FIG. 2C

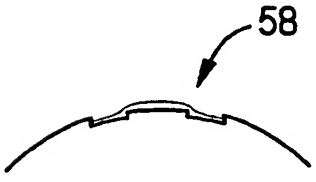

FIG. 2D

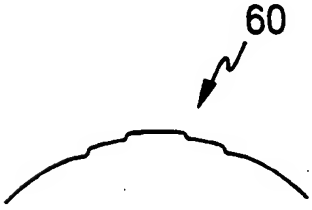

FIG. 3

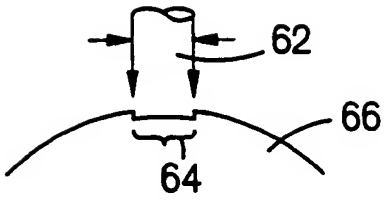

FIG. 3A

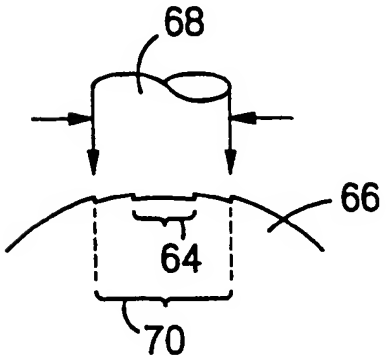

FIG. 3B

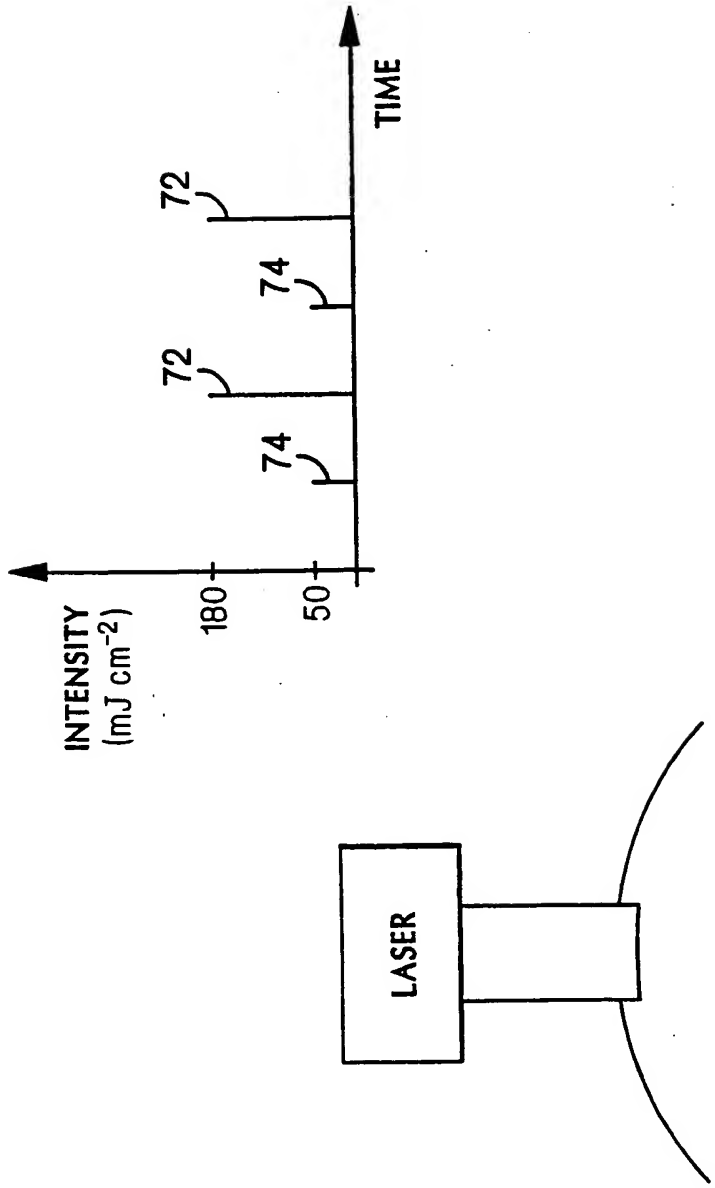

FIG. 4

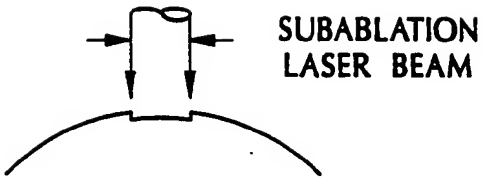

FIG. 4A

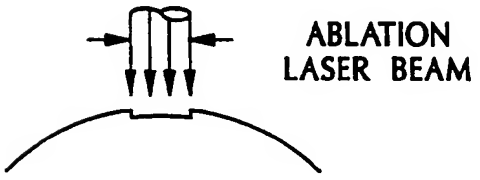

FIG. 4B

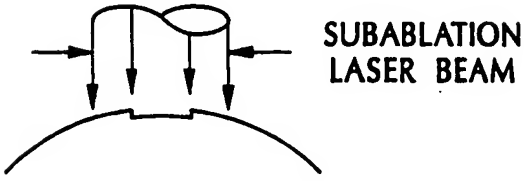

FIG. 4C

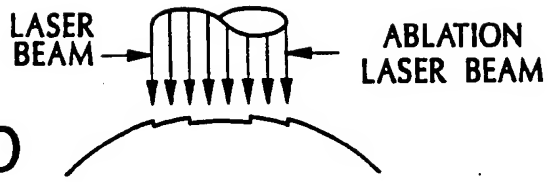

FIG. 4D

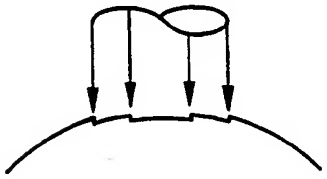

FIG. 4E

FIG. 4F

FIG. 5

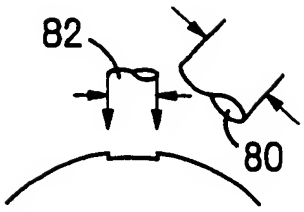

FIG. 5A

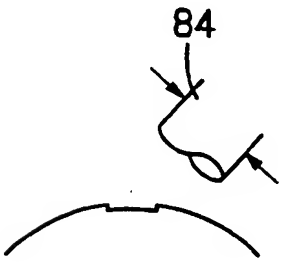

FIG. 5B

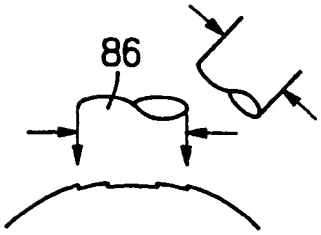

FIG. 5C

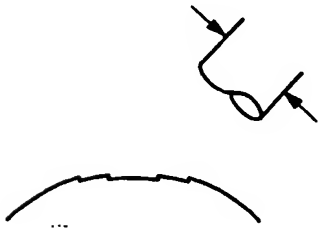

FIG. 5D

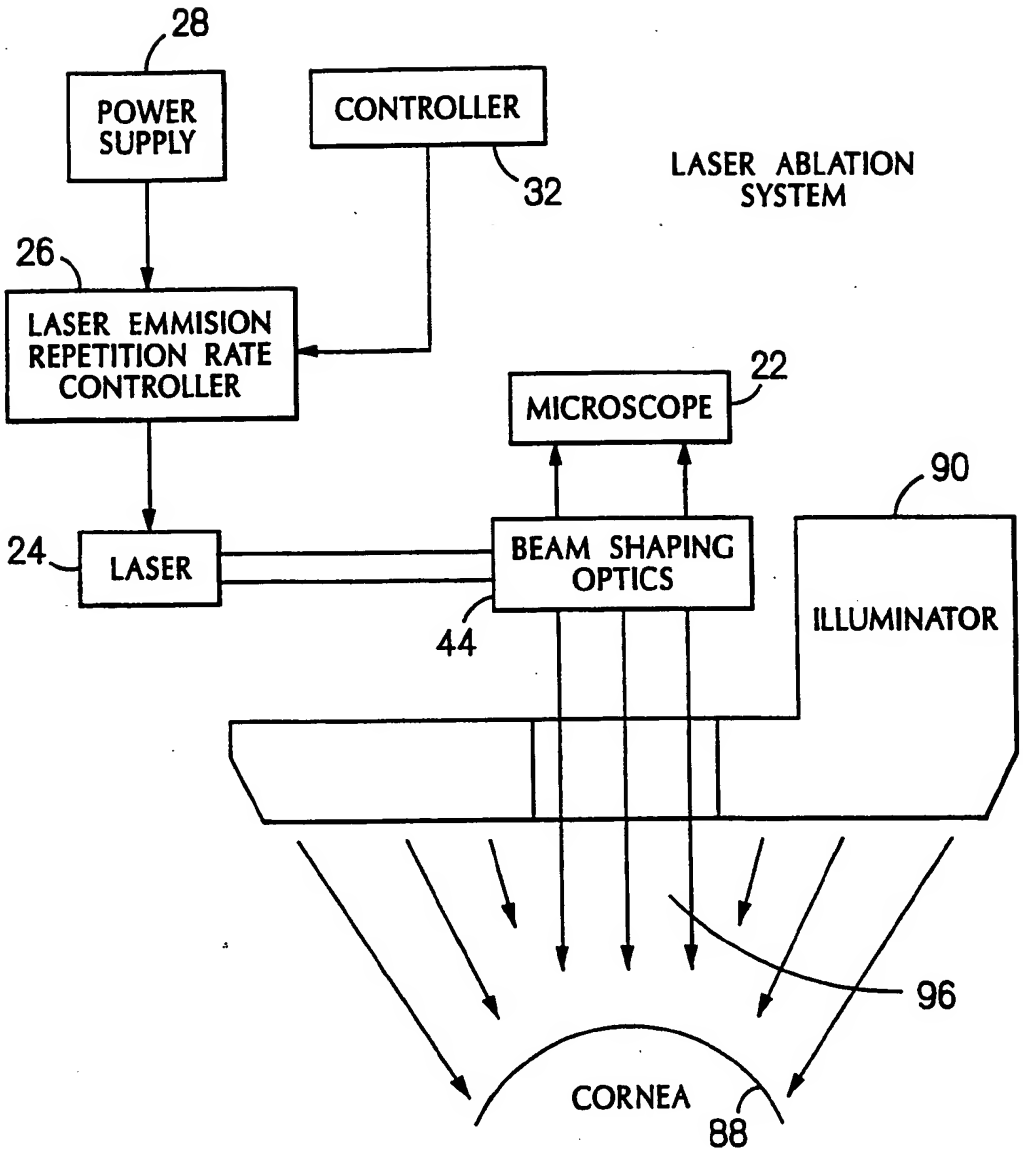

FIG. 6

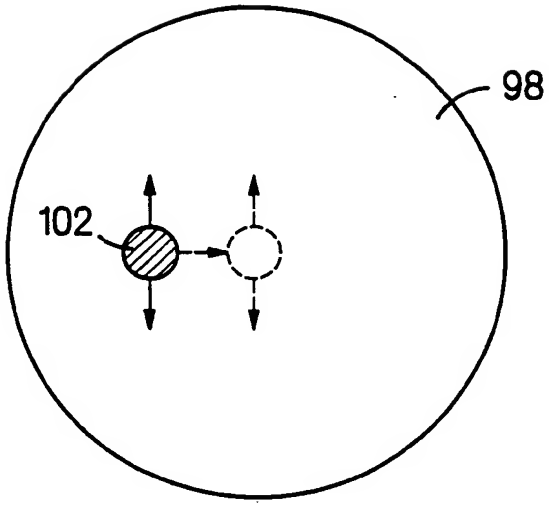

FIG. 7

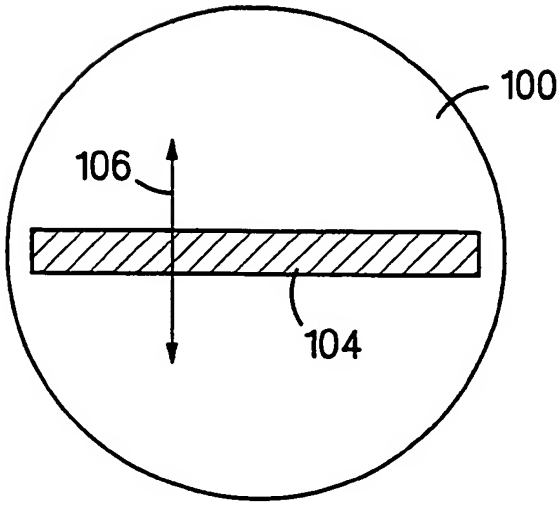

FIG. 7A

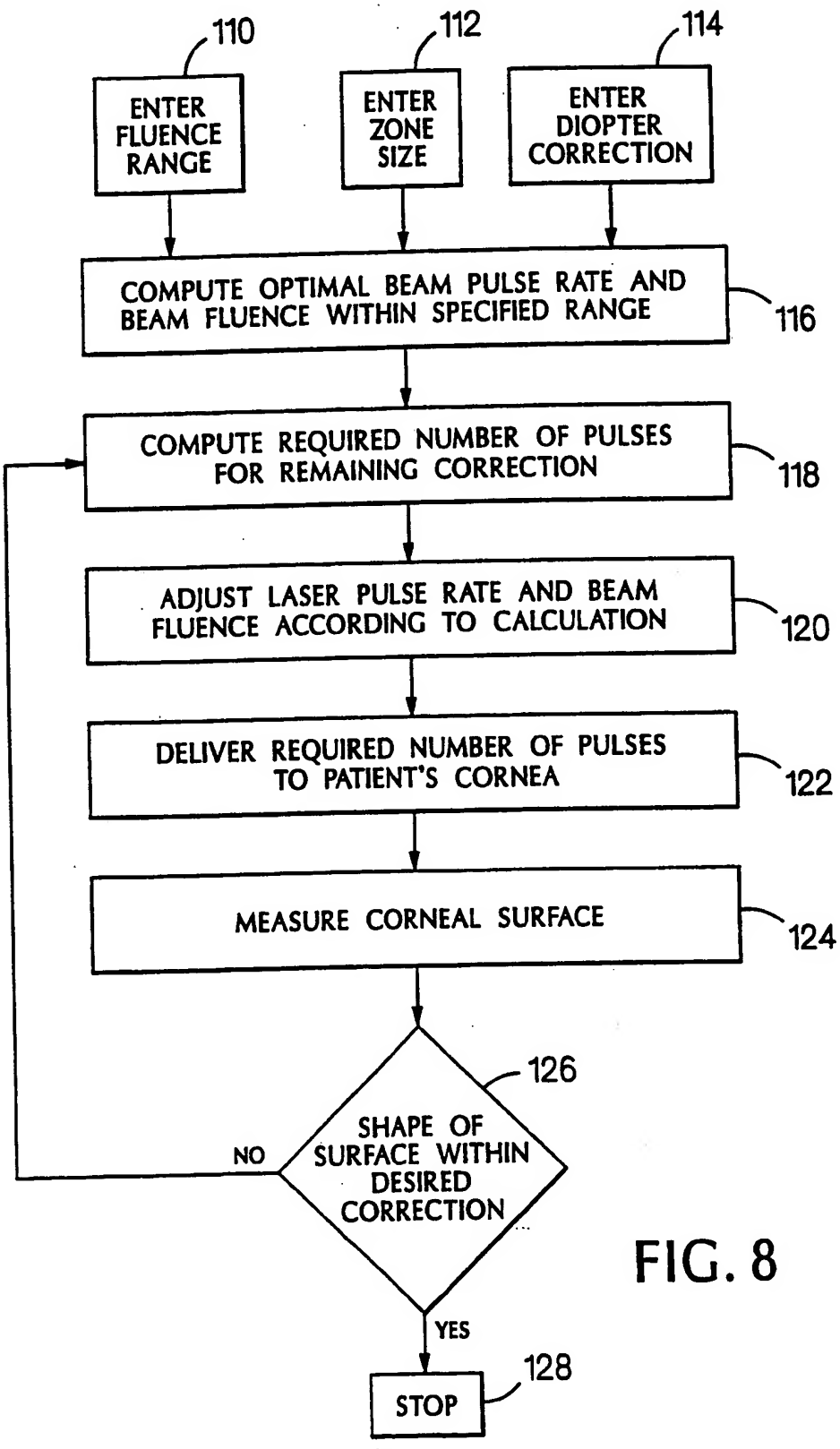
110
112
114
ENTER FLUENCE RANGE
ENTER ZONE SIZE
ENTER DIOPTER CORRECTION
COMPUTE OPTIMAL BEAM PULSE RATE AND BEAM FLUENCE WITHIN SPECIFIED RANGE
116
COMPUTE REQUIRED NUMBER OF PULSES FOR REMAINING CORRECTION
118
ADJUST LASER PULSE RATE AND BEAM FLUENCE ACCORDING TO CALCULATION
120
DELIVER REQUIRED NUMBER OF PULSES TO PATIENT'S CORNEA
122
MEASURE CORNEAL SURFACE
124
126
SHAPE OF SURFACE WITHIN DESIRED CORRECTION
NO
YES
STOP
128

FIG. 8

INTERNATIONAL SEARCH REPORT

Int...ational application No.
PCT/US95/04042

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61N 5/02, 5/06
US CL :606/3, 5, 10, 13
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/897, 898; 606/1-6, 10-13

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US, A, 4,718,418 (L'ESPERANCE, JR.) 12 January 1988, see entire document.	7-11, 36-41 --- 1-6, 12-35, 42

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
08 JULY 1995	24 JUL 1995
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer DAVID SHAY Stacia Simcik for Telephone No. (703) 308-2215

Form PCT/ISA/210 (second sheet)(July 1992)*